REMARKS

Applicants have received and reviewed the Final Office Action mailed on February 24, 2005. By way of response, Applicants have amended the claims. No new matter is presented. Upon entry of this Response and Amendment, claims 1, 36-42, and 44-49 will be pending. Applicants submit that the pending claims are supported by the specification, for example as indicated below.

Amendments to Claims

Claim 1 is amended to delete the phrase "an amino acid sequence having at least 99% sequence identity".

Claim 3 is canceled as duplicative of amended claim 1.

Claim 39 is amended to present the claim in independent form.

Claim 40 is amended to replace the phrase "and which binds to an antibody that specifically binds a polypeptide comprising the sequence of SEQ ID NO:4" with --wherein the polypeptide comprises one or more membrane spanning domains--. Basis for this amendment is found in the specification and claims, as originally filed, for example, at page 14, lines 11-14.

Claim 43 is canceled as duplicative of amended claim 39.

Claim 44 is amended to require the claimed polypeptide to comprise sequences of SEQ ID NO:2 and SEQ ID NO:4.

Claim 45 is amended to depend from independent claim 36 and to require the polypeptide to further comprise SEQ ID NO:2.

Claim 47 is amended to delete the term "yellow fluorescent protein".

Rejections under 35 U.S.C. § 101 and 35 U.S.C § 112, first paragraph

Claims 1, 3, and 35-49 are rejected as allegedly lacking support by either a specific asserted utility or a well established utility. Applicants respectfully traverse this rejection. Although this rejection has not been raised for the newly presented claims, it is discussed insofar as it might apply.

The Utility Requirement

A "specific utility" is *specific* to the subject matter claimed. MPEP § 2107.01. Specific utility is established, for example, where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. *Id.* Applicants respectfully submit that the specification supports the specific utility of the claimed subject matter for the reasons provided below.

Independent claims 1, 39, 40, and 44 are generally directed to isolated polypeptides comprising the sequence of SEQ ID NO:2 and/or of SEQ ID NO:4. SEQ ID NOs:2 and 4 are polypeptide fragments of hSTRA6. Applicants have demonstrated that hSTRA6 has a specific biological activity in that hSTRA6 is a part of the Wnt signal transduction pathway (see page 4, lines 20-25 and Example).

Applicants submit that at the time the application was filed (March 23, 2001), it was known that the Wnt signal transduction pathway was involved in human cancer (See for example, Polakis, 2000, *Genes Dev.* 14:1837-1851, "Wnt singaling in cancer"; Smalley *et al.*, 1999, *Cancer Metastasis Rev.* 18:215-30, "Wnt signaling in mammalian development and cancer"). Polakis and Smalley teach that Wnt activation causes β-catenin to persistently activate transcription factors such as TCF and LEF. Smith *et al.* 1999 (*Br. J. Cancer* 81:496-502) teaches that β-catenin, part of the Wnt pathway, is involved in colon cancer. Moreover, Applicants submit that it was well known at the time the application was filed that effective treatments for cancer include treatments that interrupt oncogenic signal cascades such as the Wnt signal transduction pathway. See, for example, Woodburn, 1999, *Pharmacol Ther*, 82:241-250.

As discussed in the prior response, the inventors have identified an important downstream cellular component of the Wnt-1 signaling pathway in mammary cells transformed by Wnt-1, solving the problem of downstream Wnt-1 targets. Using the Wnt-1 expressing C57MG mouse mammary epithelial cell model, STRA6 was identified as an upregulated gene. These results were confirmed by QEA analysis, that demonstrated upregulation of STRA6 in Wnt-1 epressing cells (11-fold higher than wild-type or Wnt-4 expressing cells). This showing of differential expression regulated by Wnt-1 expression, reasonably demonstrates STRA6 as a candidate gene for diagnosis and therapeutic use in Wnt related cancer. A diagnostic assay based on differential expression of STRA6 as compared with a control is supported by the teachings of the specification. See, for example, page 1, lines 23-26; page 4, lines 20-25; and page 15, lines 4-14.

Applicants submit that at least one specific utility for the claimed subject matter has been established because the claimed polypeptides have a specific biological function in the Wnt signal transduction pathway. The claimed polypeptides are shown to be a part of the Wnt signal transduction pathway, known to be involved in cancer. Because it was well known at the time the application was filed that the Wnt signal transduction pathway was involved in cancer, for example colon cancer, Applicants submit that one of skill in the art would reasonably correlate the claimed polypeptides with cancers related to Wnt.

Moreover, Applicants submit that the claimed subject matter has substantial utility because of the real world use of the claimed polypeptide in the diagnosis or detection of cancer. As noted above, the application establishes that Wnt upregulates expression of the claimed polypeptides. Since Wnt upregulation is indicative of cancer, upregulaton of the claimed polypeptides reasonably correlates to an indication of Wnt-induced cancer.

In the Office Action mailed on March 17, 2003 (Paper No. 17), the Examiner argues that neither the specification or any art of record teaches what the hSTRA6 polypeptide is, how it functions, or a specific and well-established utility or the involvement in the etiology of any specific disease. Applicants respectfully disagree for

the reasons provided above. Additionally, Applicants submit that there is no requirement that the claimed subject matter be fully characterized to be patentable. Applicants have provided an enabling disclosure commensurate with the scope of the claims. Applicants have also established patentable utility for the claimed subject matter. Thus, Applicants submit the rejection is overcome.

In the February 2005 Office Action and Paper No. 17, the Examiner also argues that protein sequence homology alone does not permit extrapolation to an isolated amino acid's biological function or uses thereof. Applicants submit the instant application has provided more than sequence homology. Applicants have demonstrated that the claimed polypeptides are involved in the Wnt signal transduction pathway, a known cancer pathway. Applicants submit that the role of the claimed polypeptides in a well-known cancer pathway is itself a biological function independent of the disclosed sequence data.

In Paper No. 17, the Examiner also argues that the specification is an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide. Applicants respectfully disagree. Applicants point out the pending claims do not require one of skill in the art to discover a functional use of the claimed polypeptide because the specification discloses that the claimed polypeptides can be used to detect Wnt related cancers or to produce antibodies that are useful in diagnostics for the detection of Wnt related cancers. Applicants submit that it is not necessary to fully characterize the claimed polypeptides for the polypeptides to have patentable utility. For example, it is not necessary that a target, if any, of the claimed polypeptides be identified. The sequence data alone provides sufficient information.

In the Office Action mailed on November 11, 2003 (Paper No. 20), the Examiner argues post-filing date references cannot be used to determine whether the specification is enabling. Applicants submit that the post-filing date references corroborate the utility asserted in the specification. The Examiner appears to question the credibility of the asserted utilities. Applicants have submitted post-filing date references to emphasize the credibility of the utility asserted in the specification at the time of filing. Additional references such as He *et al.*, 2005, *Oncogene*, online

publication, "Blockade of Wnt-1 signaling induces apoptosis in human colorectal cancer cells containing downstream mutations" demonstrate recognition in the art that interruption of the Wnt signal transduction signal can have a therapeutic role in the treatment of cancer, for example colorectal cancer.

In Paper No. 20, the Examiner also argues that expression levels of mRNA do not necessarily correlate or predict equivalent levels of polypeptide expression, and cites references relating to p53 expression and cholinephosphate cytidylyltransferase. Applicants respectfully submit that this argument is inapplicable. First, the Examiner fails to present references relating to the Wnt pathway. How proteins other than those in the Wnt pathway are expressed is immaterial to the present application. Moreover, the present specification establishes a reasonable correlation between increased mRNA levels of the claimed polypeptides and involvement in a known cancer signal transduction pathway, the Wnt pathway. The Office Action alleges that to be a diagnostic, the expression pattern of the claimed polypeptides must be present only in cancer tissue and not in normal tissue. Applicants respectfully disagree. Many genes are expressed in both normal and cancerous tissue, and the ability to detect or diagnosis cancer can be achieved by comparing expression patterns of a specific gene in test samples to controls.

The state of the art at the time the specification was filed indicated that Wnt signaling causes cancer (See, for example, Polakis, 2000, *Supra*). The specification establishes that Wnt signaling causes an increase in expression of the claimed polypeptides. Applicants submit that the difference in expression levels of the claimed polypeptides between test samples and controls can be used to detect or diagnose Wnt-related cancer (See, for example, p. 70, lines 19-23).

For at least the reasons discussed above, Applicants submit the asserted diagnostic utility for hSTRA6 is specific, substantial, credible, and fully supported by the specification. An assertion of utility is credible unless the logic underlying the assertion is seriously flawed, or the facts upon which the assertion is based are inconsistent with the logic. No such showing has been made by the Examiner. The asserted utility is specific: hSTRA6 differential expression compared to controls specifically relates to

cellular transformation and cancer diagnosis. The asserted utility is substantial: cancer diagnosis is a substantial part of today's health concerns, as this serious illness claims many lives each day. In view of the specific, substantial, and credible disclosure provided by the specification, and the Examiner's failure to show any inconsistency or flaws in the asserted facts or logic, removal of this rejection is requested.

Applicants assert the requirements of § 101 are met. Because the specification meets the utility requirement, Applicants assert one of skill in the art would know how to make and use the claimed invention, as taught by the specification. Withdrawal of the § 101 and § 112, 1st paragraph rejections is requested.

Written Description

Claims 1, 36-38, and 40-49 are rejected as allegedly lacking written description. Applicants respectfully traverse this rejection. Although this rejection has not been raised for the newly presented claims, it is discussed insofar as it might apply.

As discussed above for utility and enablement, and in the prior responses, Applicants assert the specification provides sufficient teaching, correlations, and description of the claimed hSTRA6 and its use, for example in the diagnosis of cancer. Furthermore, Applicants disclose two peptide fragements of human STRA6 and correlate these sequences to a known murine STRA6 sequence. One of skill in the art, following well known principles, would be under no undue burden to produce and use the claimed polypeptides. A description is presumed to be adequate unless sufficient evidence or reasoning to the contrary is presented. Compliance with the written description requirement does not require the subject matter to be exactly described, but requires a showing that one skilled in the art would recognize the applicant had invented what was claimed. (MPEP 2163.02).

Written description requires a precise definition by structure, formula...sufficient to distinguish the claimed invention from other materials. A formula is normally adequate. (*Univ. California v. Eli Lilly and Co.*, 43 USDQ 2d 1398, 1405 (Fed. Cir. 1997). Because the sequences of the claimed hSTRA6 polypeptides is provided in Table 2 (SEQ ID NO:2) and 4 (SEQ ID NO:4) (pages 35-36), and variants of these are

taught and also described by formula (page 21, lines 28-31), Applicants assert the claimed invention is adequately described.

Additionally, the specification explicitly teaches preferred modifications of the claimed polypeptides at page 24, line 28 through line 18 of page 26, Table A, and Table B. In view of these teachings in the specification, Applicants submit the claims are fully described in the specification. Removal of this rejection is requested.

With regard to claim 47, Applicants deleted the term "yellow fluorescent protein". In view of this amendment, the rejection is overcome.

Anticipation

The Examiner has rejected claim 1 as anticipated by any one of six references:

1) U.S. 2002 0156 52A1 dated 1/13/00
2) U.S. 20021703461A1 dated 1/13/00
3) U.S. 20030149239A1 dated 1997, 1998
4) U.S. 20030187201A1 dated 1997, 1998, 1999
5) U.S. 20030187202A1 dated 1997, 1998, 1999
6) U.S. 20030187203A1 dated 1997, 1998

To the extent this rejection is maintained against the polypeptide comprising the sequence of SEQ ID NO:2 recited in amended claim 1, Applicants respectfully traverse. A sequence comparison between the claimed SEQ ID NO:2 the closest sequence disclosed in the cited references (SEQ ID NO:2 of references 1 and 2; and Figue 80 of references 1-6) shows one (1) mismatch between the two sequences and one (1) conservative substitution out of 198 amino acids or approximately 99% sequence identity. Applicants further submit that references 2-6 (as above) do not appear to disclose even the mismatched polypeptide in any priority document that would provide a proper basis for a 102(e) rejection.

Applicants have amended claim 1 to be directed to a polypeptide comprising SEQ ID NO:2. Because the cited references fail to disclose SEQ ID NO:2, Applicants respectfully submit that the rejection is overcome.

Conclusion

In view of the above amendments and remarks, Applicants respectfully request reconsideration and a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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